Remarks

I. Status of the Claims

Claims 1-34 are pending in the application, with claims 1 and 2 being the independent claims.

II. Summary of the Office Action

In the Office Action dated October 25, 2001, the Examiner has made one claim objection and one rejection of the claims. Based on the following remarks, Applicants respectfully request that the Examiner reconsider all outstanding objections and rejections and that they be withdrawn.

III. Claim Objection

The Examiner has objected to claim 22 as being dependent upon a rejected base claim. *See* Paper No. 11, page 2. The Examiner stated that claim 22 would be allowable if rewritten in independent form including all of the limitations of the base claim and any intervening claims. *See id.* As discussed in detail below, Applicants traverse the rejection of the claims from which claim 22 depends. Accordingly, Applicants submit that the objection to claim 22 as being dependent upon a rejected base claim is moot and should be withdrawn.

IV. Claim Rejections -- 35 USC § 102

The Examiner has rejected claims 1-21 and 23-34 under 35 USC § 102(e) as being anticipated by Singer, U.S. Patent No. 5,824,787. *See* Paper No. 11, page 2. Applicants respectfully traverse this rejection.

In the previous Office Action, the Examiner contended that:

> Singer teaches compositions and methods for determining the size of a nucleic acid molecule, comprising the transformation into and subsequent expression in a host cell of a vector comprising a nucleic acid molecule which comprises two or more repeating sequences separated by a restriction site, which repeating sequences comprise single identical or non-identical nucleotides and their complement, which repeating sequences conform to the formulae: $(X_1X_2)_n$ (and its complement), whereby X_1 and X_2 are single nucleotides and n is an integer from 1 to 1 x 10^{10}; or $(X_1X_2)_nA_m$ (and its complement $B_m(Y_1Y_2)_n$, whereby X_1, X_2, A and B are single nucleotides, n is an integer from 1 to 1 x 10^{10}, and m is an integer between 1 and 100, wherein two or more repeating sequences are separated by restriction endonuclease cleavage into repeats including monomers through pentamers, which resulting nucleic acid ladder is detectable using a detectable label such as a chemiluminescent label.

Paper No. 6, pages 6-7 (citation omitted).

In response to these contentions, Applicants noted that Singer does not anticipate the present claims because Singer does not disclose all of the elements of the present claims. *See* Paper No. 8, filed March 20, 2001. In particular, Singer does not teach a nucleic acid molecule wherein the top and bottom strands have substantially identical base compositions. *See* Paper No. 8, page 11. Applicants also pointed out that the molecules specifically exemplified in Example 2 at cols. 11-13 and in Fig. 2 of Singer, and referred to in Singer as "the prototypic embodiment" of the invention disclosed therein, do not contain substantially identical base compositions in the top and bottom strands.

In responding to Applicants' assertions, the Examiner now contends that:

> [t]he examples provided in the instant specification of substantially identical base compositions comprise approximately 60% sequence identity (See page 8 of the specification, lines 16-24). In the examples provided by Singer, nucleic acid molecules comprising approximately 60% sequence identity between the bottom and top strands are listed (See especially element design *EP/SmP* in Table 1 of Singer, in columns 11 and 12). Therefore the examples provided by Singer anticipated the claimed invention.

Paper No. 11, page 3.

From the foregoing statement, it appears that the Examiner has misunderstood the meaning of top and bottom strands having *nucleotide compositions* that are "substantially identical" to one another. More specifically, it appears that the Examiner has confused the concept of *nucleotide composition* with that of *nucleotide sequence identity*. Since the present claims do not contain any limitations as to nucleotide sequence identity but only refer to sequence composition, the Examiner's comments regarding nucleotide sequence identity are irrelevant in an analysis of anticipation under 35 USC § 102.

Applicants note that the meaning of "substantially identical in base composition" is set forth in the specification as follows:

> By "substantially identical in base composition" is meant that the top and bottom strands of the repeat-containing sequence are about 80%, preferably at least about 90%, more preferably at least about 95%, still more preferably at least about 98% or about 99%, and most preferably at least about 100%, identical in *base composition*.

Specification at page 8, lines 7-11 (emphasis added). Moreover, as understood by persons of ordinary skill in the art, the term "base composition" refers to the relative proportion of each nucleotide base (A, C, G and T) in a given nucleotide sequence. Thus, the concept of

"sequence identity," as discussed by the Examiner, is distinct from the concept of "base composition," as recited in the present claims.

The significance of base composition in the context of the present invention is clearly set forth in the specification:

> The migration of nucleic acid fragments on polyacrylamide gels is influenced by nucleotide base composition as well as size; that is, two nucleic acid bands containing the same number of base pairs but different nucleotide base compositions may migrate differently on polyacrylamide gels. According to the present invention, the base composition of the top strand of the repeat of the ladder is substantially the same as the base composition of the bottom strand, so the two nucleic acid strands will migrate identically when separated on denaturing polyacrylamide gels.

Specification at page 16, lines 4-11.

With the above discussion in mind, Applicants restate their assertion that Singer cannot and does not anticipate the present claims because Singer does not teach a nucleic acid molecule wherein the top and bottom strands have substantially identical base compositions. For example, the sequence element designated "EP/SmP" in Singer has the following nucleotide sequence:

GTT GTG TGG GGG GTT TTT AG.

The base composition of this (top) sequence is 5% A, 0% C, 50% G and 45% T. In double-stranded form, the complementary (bottom) strand of EP/SmP would have the following sequence:

CAA CAC ACC CCC CAA AAA TC.

The base composition of this bottom strand is 45% A, 5% C, 0% G and 5% T. Thus, the base composition of the top strand of EP/SmP in Singer is *not* substantially identical to the

base composition of the corresponding bottom strand. In fact, the base compositions of these two strands are completely different from one another.

By contrast, the exemplary repeat-containing sequences of the present invention that are set forth in the specification at page 8 exhibit *identical* top and bottom strand base compositions. For example, SEQ ID NO:1 (ATC TCA GGA T) has the following base composition: 30% A, 20% C, 20% G and 30% T. The complementary (bottom) strand (TAG AGT CCT A) has the *same* base composition, that is, 30% A, 20% C, 20% G and 30% T. As the specification makes clear, this identity of base composition is of great significance in determining the manner in which the top and bottom strands migrate relative to one another on polyacrylamide gels.

Singer fails to expressly or inherently disclose every element of the claimed invention in a way so as to enable one of ordinary skill in the art make and use the presently claimed invention. Hence, Singer cannot and does not anticipate the present claims. Applicants accordingly request that the rejection of claims 1-21 and 23-34 under 35 USC § 102(e) be reconsidered and withdrawn.

Conclusion

All of the stated grounds of objection and rejection have been properly traversed, accommodated, or rendered moot. Applicants therefore respectfully request that the Examiner reconsider all presently outstanding objections and rejections and that they be withdrawn. Applicants believe that a full and complete reply has been made to the outstanding Office Action and, as such, the present application is in condition for allowance.

If the Examiner believes, for any reason, that personal communication will expedite prosecution of this application, the Examiner is invited to telephone the undersigned at the number provided.

Prompt and favorable consideration of this Amendment and Reply is respectfully requested.

Respectfully submitted,

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